The prevalence of memory-related issues increases with age. So does concern about dementia. Be prepared to render the best evaluation and advice possible.

James A. Wilcox, MD, PhD
Professor of Clinical Psychiatry
University of Arizona
Staff Psychiatrist
Southern Arizona Veterans Administration
Health Care System
Tucson, Arizona

P. Reid Duffy, PhD, RN
Mental Health Research Coordinator
Southern Arizona Veterans Administration
Health Care System
Tucson, Arizona

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Many older patients are concerned about their memory. The “worried well” may come into your office with a list of things they can’t recall, yet they remember each “deficit” quite well. Anticipatory anxiety about one’s own decline is common, and is most often concerned with changes in memory.1,2

Patients with dementia or early cognitive decline often are oblivious to their cognitive changes, however. Of particular concern is progressive dementia, especially Alzheimer’s disease (AD). Although jokes about “senior moments” are common, concern about AD incurs deep-seated worry. It is essential for clinicians to differentiate normal cognitive changes of aging—particularly those in memory—from early signs of neurodegenerative disease (Table 1, page 30).

In this article, we review typical memory changes in persons age >65, and differentiate these from mild cognitive impairment (MCI), an increasingly recognized prodrome of AD. Clinicians armed with knowledge of MCI are able to reassure the worried well, or recommend neuropsychological testing as indicated.

Is memory change inevitable with aging?
Memory loss is a common problem in aging, with variable severity. Research is establishing norms in cognitive functioning through the ninth decade of life.4 Controversy about sampling, measures, and methods abound,5 and drives prolific research on the subject, which is beyond the scope of this article. It has been demonstrated that there are a few
Senior moments

“optimally aging” persons who avoid memory decline altogether. Most researchers and clinicians agree, however, that memory change is pervasive with advancing age. Memory change follows a gradient with recent memories lost to a greater degree than remote memories (Ribot’s Law). Forgetfulness is characteristic of normal aging, and frequently manifests with misplaced objects and short-term lapses. However, this is not pathological—as long as the item or memory is recalled within 24 to 48 hours.

Compared with younger adults, healthy older adults are less efficient at encoding new information. Subsequently, they have more difficulty retrieving data, particularly after a delay. The time needed to learn and use new information increases, which is referred to as processing inefficiency. This influences changes in test performance across all cognitive domains, with decreases in measures of mental processing speed, working memory, and problem-solving.

Many patients who complain about “forgetfulness” are experiencing this normal change. It is not uncommon for a patient to offer a list of things she has forgotten recently, along with the dates and circumstances in which she forgot them. Because she sometimes forgets things, but remembers them later, there likely is nothing to worry about. If reminders—such as her list—help, this too is a good sign, because it shows her resourcefulness in using accommodations. If the patient is managing her normal activities, reassurance is warranted.

Mild cognitive impairment

Since at least 1958, clinical observations and research have recognized a prodrome that differentiates cognitive changes predictive of dementia from those that represent typical aging. Several studies and methods have converged toward consensus that MCI is a valid construct for that purpose, with ecological validity and sound predictive value. Clinical value is evident when a patient does not meet criteria for MCI; in this case, the clinician can reassure the worried well with conviction.

Revealing the diagnosis of MCI to patients requires sensitivity and assurance that you will reevaluate the condition annually. Although there is no evidence-based remedy for MCI or means to slow its progression to dementia, data are rapidly accruing regarding the value of lifestyle changes and other nonpharmacologic interventions.

Recognizing MCI most simply requires 2 criteria:

The patient’s expressed concern about decline in cognitive functioning from a previous level of performance. Alternately, a caretaker’s report is valuable because the patient might lack insight. You are not looking for an inability to perform activities of daily living, which is indicative of frank dementia; rather, you want to determine whether the person’s independence in functional abilities is preserved, although less efficient. Patients might repeatedly report occurrences of new problems, although modest, in some cases. Although problems with memory often are the most frequently reported symptoms, changes can be observed in any cognitive domain. Uncharacteristic inability to understand instructions, frustration with new tasks, and inflexibility are common.

Quantified clinical assessment that the patient’s cognitive decline exceeds norms of his age cohort. Clinicians are already familiar with many of these tests (5-minute recall, clock face drawing, etc.). For MCI, we recommend the Montreal Cognitive Assessment (MoCA), which is specifically designed for MCI. It takes only 10 minutes to administer.

<table>
<thead>
<tr>
<th>Table 1 Early warnings of dementia</th>
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<tr>
<td>Difficulty following sequential tasks</td>
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<td>New-onset social withdrawal</td>
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<td>An increase in word finding problems</td>
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<td>Inability to locate things due to confusion</td>
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<td>Trouble with spatial relationships</td>
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<td>New memory deficits change the actions of daily life</td>
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Source: Reference 3
Multiple versions of the MoCA, and instructions for its administration are available for provider use at www.mocatest.org.

When these criteria are met—a decline in previous functioning and an objective clinical confirmation—referral for neuropsychological testing is recommended. Subtypes of MCI—amnestic and non-amnestic—have been employed to specify the subtype (amnesic) that is most consistent with prodromal AD. However, this dichotomous scheme does not adequately explain or capture the heterogeneity of MCI.\textsuperscript{11,12} 

**Medical considerations**

Just as all domains of cognition are correlated to some degree, the overall health status of a person influences evaluation of memory. Variables, such as fatigue, test anxiety, mood, motivation, visual and auditory acuity, education, language fluency, attention, and pain, affect test performance. In addition, clinician rapport and the manner in which tests are administered must be considered.

**Depression can mimic MCI.** A depressed patient often has poor expectations of himself and slowed thinking, and might exaggerate symptoms. He might give up on tests or refuse to complete them. His presentation initially could suggest cognitive decline, but depression is revealed when the clinician pays attention to vegetative signs (insomnia, poor appetite) or suicidal ideation. There is growing evidence that subjective complaints of memory loss are more frequently associated with depression than with objective measures of cognitive impairment.\textsuperscript{13,14} 

**Other treatable conditions** can present with cognitive change (the so-called reversible dementias). A deficiency of vitamin B\textsubscript{12}, thiamine, or folate often is seen because quality of nutrition generally decreases with age. Hyponatremia and dehydration can present with confusion and memory impairment. Other treatable conditions include:

- cerebral vasculitis, which could improve with immune suppressants
- endocrine diseases, which might respond to hormonal or surgical treatment
- normal pressure hydrocephalus, which can be relieved by surgical placement of a shunt.

**Take a complete history.** What exactly is the nature of the patient or caregiver’s complaint? You need to attempt to engage the patient in conversation, observing his behavior during the evaluation. Is there notable delay in response, difficulty in attention and focus, or in understanding questions?

The content of speech is an indicator of the patient’s information processing. Ask the patient to recite as many animals from the jungle as possible. Most people can come up with at least 15. The person with MCI will likely name fewer animals, but may respond well to cueing, and perform better in recognition (eg, pictures or drawings) vs retrieval. When asked to describe a typical day, the patient may offer a vague, nonchalant response eg, “I keep busy watching the news.” This kind of response may be evidence of confabulation; with further questioning, he is unable to identify current issues of interest.

**Substance abuse.** It is essential that clinicians recognize that elders are not exempt from alcohol and other drug abuse that affects cognition. Skilled history taking, including attention to non-verbal responses, is indicated. A defensive tone, rolling of eyes, or silent yet affirmative nodding are means by which caregivers offer essential “clues” to the provider.

A quick screening tool for the office is valuable; many clinicians are most familiar with the Mini-Mental State Examination or the Saint Louis University Mental Status Examination, which are known to be sensitive in detecting memory problems and other cognitive defects. As we noted, the MoCA is now recommended for differentiating more subtle changes of MCI.\textsuperscript{10,15} It is important to remember that common conditions such as an urinary tract infection or trauma after anesthesia for routine procedures such as colonoscopy can cause cognitive impairment. Again, eliciting history from a family member is valuable
because the patient may have forgotten vital data.

A good physical exam is important when evaluating for dementia. Look for any neurologic anomaly. Check for disinhibition of primitive reflexes, eg, abnormal grasp or snout response or Babinski sign. Compare the symmetry and strength of deep tendon reflexes. Look for neurologic soft signs. Any pathological reflex response can be an important clue about neurodegeneration or space-occupying lesions. We recall seeing a 62-year-old man whose spouse brought him for evaluation for new-onset reckless driving and marked inattention to personal hygiene that developed over the previous 3 months. On examination, he appeared disheveled and had a dull affect, although disinhibited and careless. His mentation and gait were slowed. He denied distress of any kind. Frontal release signs were noted on exam. An MRI revealed a space-occupying lesion of the frontal lobe measuring 3 cm wide with a thickness of 2 cm, which pathology confirmed as a benign tumor.

Always check for arrhythmia and hypertension. These are significant risk factors for ischemic brain disease, multiple-infarct stroke, or other forms of vascular dementia. A shuffling gait suggests Parkinson’s

| Table 2 |
| Recommendations for reducing effects of cognitive aging, from the Institute of Medicine |

| Engage in physical activity |
| Reduce and manage cardiovascular risk factors |
| Regularly review health conditions and medications that might affect cognitive health |
| The committee suggested 3 additional actions supported by some scientific evidence to suggest positive effects on cognition: |
| • Pursue intellectual engagement, with ongoing opportunities to learn |
| • Get adequate sleep |
| • Avoiding the risk of cognitive changes due to delirium if undergoing procedures or hospitalization |

Source: Reference 22

Clinical Point
Cerebral atrophy, space-occupying lesions, and shifting of the ventricles often correspond with cognitive decline.

Presentation, Diagnosis, and Treatment

This monthly newsletter series focuses on issues in proper diagnosis and management of adult patients with bipolar disorder. Each of the 3 monthly newsletters reviews a specific challenge and presents a fictional patient case with expert commentary to help healthcare professionals make informed treatment decisions.

Each newsletter features commentary by Henry A. Nasrallah, MD.
Take a medication history. Many common treatments for anxiety and insomnia can cause symptoms that mimic dementia. Digitalis toxicity results in poor recall and confusion. Combinations of common medicines (antacids, antihistamines, and others) compete for metabolic pathways and lead to altered mental status. Referencing the Beers List is valuable; anticholinergics, benzodiazepines, and narcotic analgesics are of special concern. The latter could still be useful for comfort care at the end of life.

It is common for seniors to take a variety of untested and unproven supplements in the hope of preventing or lessening memory problems. In addition to incurring significant costs, the indiscriminate use of supplements poses risks of toxicity, including unintended interactions with prescribed medications. Many older adults do not disclose their use of these supplements to providers because they do not consider them “medicine.”

**Treatment**

Effective treatment of dementia remains elusive. Other than for the “reversible dementias,” pharmacotherapy has shown less progress than had been expected. Donepezil, galantamine, rivastigmine, and memantine could slow disease progression in some cases. There have been many studies for dementia preventives and treatments. Extensive reviews and meta-analyses, including those of randomized controlled trials abound for a variety of herbs, supplements, and antioxidants; none have shown compelling results. Table 2 (page 33) lists Institute of Medicine recommendations supported by evidence that could reduce effects of cognitive aging.

Recommendations from collaboration between the National Institute on Aging and the Alzheimer’s Association state that research should focus on biomarkers, such as neural substrates or genotypes.

**Bottom Line**

Variations in cognition occur over the lifespan. Be aware that mild cognitive impairment (MCI) is not a benign change but a harbinger of dementia for most affected people. We are able to differentiate the worried well from patients with MCI. The importance of early treatment for reversible forms of dementia is vital to reducing patient suffering and the overall burden on caregivers. Early identification of MCI will assist further research toward prevention or delay of progression to Alzheimer’s dementia.

**Related Resources**


**Drug Brand Names**

Donepezil - Aricept  
Memantine - Namenda

Galantamine - Reminyl  
Rivastigmine - Exelon

**Labs.** The next level of evaluation calls for a basic laboratory workup. Check complete blood count, liver enzymes, thyroid function tests, vitamin D, B₁₂, and folate levels; perform urinalysis and a complete metabolic panel. Look at a general hormone panel; abnormal values could reveal a pituitary adenoma. (In the past 33 years, the first author has found 42 pituitary tumors in the workup of mental status change.)

We use imaging, such as a CT or MRI of the brain, in almost all cases of suspected dementia. Cerebral atrophy, space-occupying lesions, and shifting of the ventricles often correspond with cognitive decline.

**Clinical Point**

Other than for the ‘reversible dementias,’ pharmacotherapy has shown less progress than had been expected.
Indicators of oxidative stress (cytokines) and inflammation (isoprostanes) show promise as measures of brain changes that correspond with increased risk of AD or other dementias.

**Summing up**

Older adults are a heterogeneous group. Intellectual capacity does not diminish with advancing age. Many elders now exceed expectations for productivity, athletic ability, scientific achievement, and the creative arts. Others live longer with diminished quality of life, their health compromised by progressive neurodegenerative disease.

Age-associated memory change often is exaggerated and feared by older adults and, regrettably, is associated with inevitable functional impairment and is seen as heralding the loss of autonomy. The worried well are anxious, although the stigma associated with cognitive decline may preclude confiding their concerns.

Providers need the tools and acumen to treat patients along an increasingly long continuum of time, including conveyance of evidence-based encouragement toward optimal health and vitality.

**References**


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**Clinical Point**

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